Women and Ischemia Syndrome Evaluation (WISE)
Diagnosis and Pathophysiology of Ischemic Heart Disease
Workshop

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Session 7

1. Topic and Author

New Frontiers in Detection of IHD in Women.

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2. Where we stand in 2002. Overview/rationale for inclusion of topic.

The prognostic implications of the diagnosis of ischemia vary drammatically in different clinical ischemic syndromes. At one extreme end, in unstable angina the detection of ischemia indicates the persistence or recurrence of instability, hence carries much more severe prognostic implications than in chronic stable angina. At the other extreme, in patients with microvascular angina the detection of ischemia does not indicate an increased risk of infarction or of sudden cardiac death and becomes clinically relevant only if its causes can be understood and effectively treated.

A typical condition in which the diagnosis of myocardial ischemia is difficult is the so-called cardiac syndrome X. This syndrome, which includes 60-70% of women (about 60% post-menopausal and 40% pre-menopausal) but also 30-40% of men, is characterized by angina pectoris and normal coronary angiography. Its incidence may vary from 10% to 50% of patients submitted to coronary arteriography.

Action 1. Such broad inclusion criteria confuse the issue, because of the likely inclusion of heterogeneous patients with and without a cardiac origin of pain. The selection of patients who present with specific patterns of clinical symptoms and with transient ischemic ECG changes during chest pain would lead to more homogeneous subgroups as the association of anginal pain with transient ECG changes indicates a cardiac, although not necessarily an ischemic origin of pain. Moreover distinct patterns of clinical presentation might correspond to different specific pathogenetic mechanisms. (1)

Several studies focusing on this specific subgroups of patients have shown findings consistent with a patchily distributed coronary microvascular dysfunction, sufficient to cause chest paint, ECG changes and in some cases, perfusion abnormalities during effort tests, but not confluent and severe enough to cause detectable contractile dysfunction or lactate production: (2)

- reproduction of typical pain with the dipyridamole test, usually with tipical ischemic changes but no contraction abnormality (3);
- worsening of the result of the exercise test following sublingual nitrates (4), consistent with the frequent clinical report of a poor response to sublingual nitrates;
- ischemic myocardial metabolic changes by MRS (5);
- release of lipid proxidation products in the coronary sinus at the end of pacing induced ischemic changes (6).

The causes of this coronary microvascular dysfunction may be multiple, as suggested by the total absence of MIBG cardiac uptake in over 50% of the cases, by a regional defect corresponding to the site of thallium defects in about 25%, and by totally normal uptake in the remaining 25% (7).

In spite of the absence of increased risk of infarction and cardiac death, these patients may be crippled by pain. The inconsistent response to nitrates and antianginal drugs, indicates the need for research on the various potential causes of coronary vascular dysfunction, in order to develop rational forms of therapy.

3. Current challenges and the most important issues for future research

The new avenues of research

We are engaged in a program of outcome research on all patients presenting to our department with their very first manifestation of IHD. Following informed consent, they are administered a computerized, standardized questionnaire, focusing on possible differences in symptoms and presentation for each of the various ischemic syndromes; a blood sample is obtained for traditional risk factors, proteomic studies, mRNA from lekocytes and platelets and for genomic DNA and is stored in biological banks. Within each clinically defined homogeneous subgroup, all patients undergo tests and interventions as clinically required, and selected ones are also ivolved in special pathogenetic studies. All enter in a regular follow up program, which will identify patients with different outcomes. Correlations between outcome and blood tests on admission, will allow us to obtain novel information on pathogenetic mechanisms, predisposing and protective factors, useful for developing novel, rational treatment strategies.

Future Clinical Research Directions

1. The main thrust of research in the field of IHD has been the identification of common mechanisms of disease and of average prognostic determinants for combined, mixed events.

2. Even within such a broad research framework, epidemiological, post-mortem and clinical data revealed remarkable gender differences in the incidence, manifestations and diagnosis of the various syndromes that compose IHD (i.e. sudden ischemic cardiac death, unheralded acute infarction, acute infarction preceeded by unstable angina, as well as in stable, unstable, variant and microvascular angina). In particular epidemiological studies consistently show that, in contrast with infarction, the age-related incidence and prevalence of angina is nearly similar in both genders, and that the very first clinical manifestation of IHD is more often with infarction in man and with angina in women.

3. The new frontiers of research in the multiple syndromes that compose IHD is the identification of the actual causes for gender differences in:

- the incidence of the various ischemic syndromes and their relation to the extent and features of coronary atherosclerosis;
- the prevalence of different ischemic trigger within each syndrome.

4. Current challenges in the areas of communicating messages to health care community, patients and the public

5. Translating new findings to improved diagnosis and treatment/saving lives.

A multidimensional problem

In this general scenario, the detection of myocardial ischemia in women represents a rather marginal aspect, which becomes relevant only when ischemia is not sufficiently extensive and severe to be clearly recognized by currently available techniques – a problem that, under similar circumstances, applies also to men. In such cases it is not sufficient to diagnose the presence of ischemia but, once detected, it is also necessary to identify its actual causes, toghether with its prognosis and rational treatment strategies. A much more intriguing and complex problem is “the detection of IHD in women”. This issue requires a precise definition of each of the various syndromes that compose IHD, as indicated in the introduction.

6. References.

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